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Reply to the Editor:

We appreciate the opportunity to comment on the letter by Sortini and associates regarding our recent article on the indication for preoperative localization of small peripheral pulmonary nodules in thoracoscopic surgery.[1] We agree that intraoperative ultrasonography is noninvasive and effective in locating the solid target nodules.

We have some experience with intraoperative ultrasonographic examination with an ultrasound scanner (B&K Medical, Gentofte, Denmark) with a linear scan multifrequency probe (5-7.5 MHz), and we encountered the same limitations in patients as those faced by Sortini and colleagues.[2] Chief was difficulty in obtaining an image as long as any air remained in the lung, caused by an incomplete lung collapse. Visualizing pulmonary lesion by ultrasonography requires complete collapse of the lung, which is often impossible in patients with obstructive disease such as emphysema. Formless abnormalities may be particularly difficult to visualize. In our experience, intraoperative ultrasonography is effective in locating the multiple solid pulmonary nodules, such as multiple metastatic pulmonary tumors. On the other hand, small and deep nodules may be missed by ultrasonography. Especially soft nodules, such as localized bronchioloalveolar cell carcinoma (BAC), could be more difficult to separate from normal but collapsed lung because the image is soft, small, faint and of similar consistency to the surrounding normal lung parenchyma. BAC shows a replacement growth of atypical cells with mild thickening of the alveolar septa, sometimes without fibrotic foci.[3] BAC is not uncommon; it actually accounted for 45% (n = 32/71 patients) of the adenocarcinoma seen during our study. In such cases, preoperative localization can be more effective. The technical differences mentioned may explain in part the poor yield of ultrasonography in our hands in distinguishing BAC. It is generally accepted, however, that localization with intraoperative ultrasonography has several limitations.[4,5]

From a practical standpoint, we use a preoperative localization technique because at our institution most small pulmonary nodules that require localization are BAC. The procedure is safe and accurate, and we believe that the requirement for preoperative localization will remain as long as the application of thoracoscopic surgery increases. Thus discussion of the indications for preoperative localization is still important.

Again, we agree that intraoperative ultrasonography is effective in selected cases in our experience. We need to make the right choice of localizing method in each case for minimally invasive surgery.

Hajime Saito, MD
Yoshihiro Minamiya, MD
Jun-ichi Ogawa, MD
Second Department of Surgery
Akita University School of Medicine
Akita City, Japan

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Negative aspects of preoperative delay in early stage non–small cell lung cancer

To the Editor:

We would like to express or opinion about the article of Quarterman and associates,[1] "Effect of Preoperative Delay on Prognosis for Patients With Early Stage Non–Small Cell Lung Cancer." We think that in this work there are some negative aspects. The first is based on the assumption that larger tumors are larger because they are more aggressive. So if you diagnose a solitary pulmonary nodule of 2 cm diameter and if the contention that "larger tumors might present as larger tumors because they are more aggressive and not simply because they are older"[1] is biologically true, is the nodule that you have diagnosed an older less aggressive nodule or an aggressive nodule in early phase? If the nodule diagnosed is an aggressive nodule in the early phase, is it acceptable to take a "watch and wait" approach, or, without any histologic findings from less invasive methods, is prompt surgery a better option? Until it can be ascertained that a nodule is nonaggressive without a histologic diagnosis, we prefer the surgical approach.

The second negative aspect in the work of Quarterman and associates[1] is the cutoff between diagnosis and delayed resection. We think that no surgeon should wait so long for perform a surgical operation in a patient with the diagnosis of solitary pulmonary nodule. In fact, isn't the correct cutoff 90 days, because the maximum delay between diagnosis and treatment is 10 or 15 days? We therefore consider it wrong to compare patients operated on within 90 days and at least 90 days after presentation. It would be more correct to compare patients operated on within 15 days and patients operated on at least 90 days after diagnosis. We think that the watch and wait approach is not the best choice. We prefer the surgical approach, because the survival after surgical resection improves dramatically for stage 1A; in fact, for primary lesions smaller than 3 cm with no nodal spread, the 5-year survival approaches 70% to 80%.[2] For us the surgical approach for solitary pulmonary nodules is the criterion standard even for patients with a history of malignancy,[3] for whom an immediate histologic diagnosis is still more important. We do apply the watch and wait approach,

but only for well-selected patients (young, without history of malignancy or smoking, with a nodule radiologic pattern of benignity or nodules with small dimension). We think that the clinician in a well-determined situation does have the option of a short watchful period.[4] But for us the watchful period doesn't last 90 days without any radiologic control; in fact our waiting period is shorter than 90 days, and every 20 days we perform a thoracic computed tomographic scan.

A. Sortini, PhD
D. Sortini, MD
G. Carrella, MD
Department of Surgical, Anaesthesiological, and Radiological Sciences
Section of Clinica Chirurgica
University of Ferrara
Ferrara, Italy

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Reply to the Editor:

My coauthors and I greatly appreciate Sortini and colleagues' comments, and we agree with their premise that prompt resection of suspicious solitary pulmonary nodules is the standard of care. However, this is a separate issue from the central conclusion of our report that there remains no good evidence to indicate that watchful waiting for selected patients worsens prognosis. This question is unlikely to be answered without a prospective trial, and we are therefore left with reasoned discussion of the evidence available.

Sortini and colleagues first take issue with our suggestion that tumor biology, and not just duration of tumor growth, may be an important factor in the observation that larger tumors are associated with a worse prognosis. Our intent was to point out that the data on tumor size and prognosis provide only circumstantial evidence for the importance of time and cannot be interpreted as proof that watchful waiting is necessarily bad. Other factors are also at play, among which tumor biology, independent of time, must be a consideration. When confronted with a nodule of low suspicion, we are then left with the question of how important time is. This leads to their second concern, that our choice of 90 days as a cutoff was inappropriate. They suggest that comparison to a group of patients who had surgery within 10 to 15 days would be more meaningful. This window is as arbitrary as any other, and 90 days was chosen for the variety of practical reasons cited in our report. Unfortunately, we are often confronted with circumstances beyond our control (such as delays in referral to a specialist, comorbidities that require evaluation and management, resource limitations that delay scheduling of necessary preoperative testing, and patient preferences) that limit our ability to bring patients to surgery expeditiously. Furthermore, we attempted to start the clock ticking with the very first chest radiograph that showed a nodule, as opposed to the date of the chest computed tomographic scan or the visit to the specialist. Thus a 15-day cutoff would be bound to produce a cohort of patients that not only would be small relative to the entire group but might also be preselected for few comorbidities and good performance status, factors that are known to favorably affect prognosis. Interestingly, Sortini and colleagues conclude by agreeing that short-term watchful waiting is appropriate in selected circumstances. Thus the optimal duration of this period remains the only open question. They have chosen 20 days, an aggressive approach that seems of questionable value.[1] As mentioned in both our report and Dr Ginsberg's accompanying commentary,[2] new computed tomography algorithms that enable volumetric modeling may permit accurate assessments of doubling times during relatively short periods (although 20 days seems ambitious).[1] The potential for this technology is exciting, but it is not yet either mature or widely available, and its value has not been demonstrated.

We hope that one day we will be able to tell with a high degree of certainty whether any given lung nodule is benign or malignant, and do so at reasonable cost with no morbidity. Until then, we must deal with the question of how much economic cost and potential morbidity are justified by the time benefit to those patients whose nodules are malignant. Unfortunately, we have so far been unable to quantify that benefit.

Mark I. Block, MD
Division of Cardiothoracic Surgery
Medical University of South Carolina
96 Jonathan Lucas St, 409 CSB
Charleston, SC 29425

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Malignant status at surgical margin of limited-resected non–small cell lung cancer: A crucial finding for predicting local relapse

To the Editor:

In a recent issue, Higashiyama and colleagues[1] reported on the malignant status of the surgical margin of limited-resected non–small cell lung cancer (NSCLC). They concluded that the cytologically negative results of examination of the surgical margin by the technique of intraoperative lavage in limited surgery for lung cancer may be predict lack of local recurrence in the surgical margin. The results in Higashiyama and colleagues' study[1] are similar to those of my own investigation.[2] As such, I believe Higashiyama and colleagues' technique is also useful to find out whether NSCLC has been resected completely.

Although no recurrence on the malignant negative surgical margin was found in Higashiyama and colleagues' study,[1] I have a criticism of their technique in correcting cells on the surgical margin. It is not rare that malignant cells exist on the pleura in the naked situation[3] and after needle aspiration cytologic examination.[4] Their complicated technique was lavage cytologic examination without flooding the pleura. If the pleura is flooded for even a short while, malignant cells on the pleura contaminate it. However, it is difficult to avoid flooding the pleura with saline solution in a cup. Further, the spun cells degen-